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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/879,329	SIGNER ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,9 and 19-21* is/are allowed.

6)☒ Claim(s) *1-7 and 10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 23 December 2005 in response to the Non-Final Office Action mailed 24 June 2005. Claims 1-20 were considered in the 24 June Office Action. Claims 1-4, 6-8, 10-16 and 18 were amended and claim 21 was added in the 23 December Paper. Claims 1-21 are pending and under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 102 and 103

Rejection of claims 1 and 4 under 35 U.S.C. 102(e) as being anticipated by Bauer *et al.* U.S. Patent No. 6,534,315 and claims 1, 6, 10, 12, 14 and 15 under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* is withdrawn in view of the amendment of claim 1 such that it is directed to a genetic construct system for use in transforming host plant cells comprising host plant cells.

Claims 1, 4, 17 and 18 **stand rejected** and claims 6, 10, 12, 14 and 15 **are rejected** under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* and further in view of Ow, D. (WO 93/01283) for reasons of record and herein below. Please note that the new rejection of claims 6, 10, 12, 14 and 15 was necessitated by Applicant's amendment of claim 1 to overcome the rejection of the claims as obvious over Bauer *et al.* alone.

As described in the 1 April 2004 Office Action, Bauer *et al.* teaches a genetic construct comprising a positive selectable marker gene and a negative selectable marker gene, different in kind from the positive selectable marker, and direct repeats of a gene of interest that flank the

positive and negative selectable marker genes (see especially the paragraph beginning at line 34 in column 3 and the paragraph bridging columns 3-4). With regard to the limitation of the substrate as "complementary to" the selectable marker, Applicant indicates that this relationship is described in paragraph 30 of the specification. Based on the description therein, the limitation is understood to encompass any medium or growth condition that provides for selection by the marker gene. In columns 8-10, Bauer *et al.* contemplates a variety of positive and negative selectable marker genes and media or growth conditions that provide for selection (*e.g.*, inducers of promoters operably linked to nucleic acids encoding toxic gene products for use as negative selectable markers).

Furthermore, in the paragraph bridging columns 10-11, Bauer *et al.* teaches a method of removing a selectable marker comprising transforming cells with the genetic construct disclosed therein, identifying transformants using the integration marker (*i.e.*, positive selection marker) and then selecting cells that have lost the negative selection marker by culturing in negative selection medium. Thus, Bauer *et al.* teaches a genetic construct having all of the limitations of the genetic construct system of the instant claim 1 and a method having all of the limitations of claim 4 except that Bauer *et al.* does not teach the construct system applied to plants.

Ow teaches a method of producing marker-free transgenic plants wherein a selectable marker gene is flanked by site specific recombination sites and excised using a site specific recombinase (see especially the discussion beginning the first full paragraph on page 6 and continued through the first full paragraph on page 7).

It would have been obvious to one of ordinary skill in the art to substitute the method of Bauer *et al.*, using a construct comprising a positive and negative selectable marker flanked by

direct repeats according to the instant claims, for the method of Ow, which utilizes a selectable marker flanked by site specific recombination signals to remove selectable marker genes from plant cells. One would be motivated to modify the teachings of Ow in this way in view of the teaching of Bauer *et al.* that site specific recombination systems are inferior to the method disclosed therein because the site specific recombination does not remove all of the exogenous DNA (see especially column 3, lines 26-28).

Absent evidence to the contrary, one would have a reasonable expectation of success in practicing the method of Bauer *et al.* in plant cells because one of ordinary skill would expect that the homologous recombination required for deletion of the marker genes would operate in plant cells as well as yeast.

In view of these considerations, the instant claims 1 and 4, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made, as would the method of claim 17, which merely recites that the eukaryotic cell is a plant cell.

Finally, claim 18, which limits the cell of claim 17 to one of a variety of species, would also be obvious to one of ordinary skill in the art because Ow teaches that excision of marker genes is generally desirable in any transgenic plant (see especially the third paragraph on page 4) and explicitly contemplates production of marker-free tobacco (see especially Example 2).

For these reasons, the invention of claims 1, 4, 17 and 18 as a whole would be obvious to one of ordinary skill in the art at the time of filing.

With regard to claims 6, 10, 12, 14 and 15, the claims are directed to the genetic construct of claim 1, wherein the positive and negative selectable markers are limited to specific arrangement within the construct with respect to one another (*e.g.*, GI-PS-NS-GI *versus* GI-NS-

PS-GI). Claims 14 and 15 are further limited to comprising additional genes of interest flanking the gene of interest present as a direct repeat. As originally discussed in the 1 April Office Action (page 5), although Bauer *et al.* does not explicitly teach any particular configuration of the positive and negative selectable markers, other than that they should be flanked by the direct repeat, the skilled artisan would not expect that the arrangement of the selectable markers within the boundaries of the direct repeat would affect the function of the construct in any way.

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities because one skilled in the art would be motivated by the expectation that compounds of similar structure will have similar function (see *e.g.*, MPEP 2144.09). Thus, it would be *prima facie* obvious to the skilled artisan to use either of the configurations of positive and negative selectable markers set forth in the claims. With regard to additional genes of interest, Bauer *et al.* teaches that the constructs might comprise one or several additional genes of interest located outside of the direct repeat sequence (see especially column 4, lines 11-14).

Given these teachings, the invention of claims 6, 10, 12, 14 and 15, as a whole, would also have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

The remarks filed 23 December 2003 do not specifically address the rejection of the claims as obvious over Bauer *et al.* and further in view of Ow. In the discussion bridging pages 7-8 of the remarks, Applicant does contend that the amended claims are distinguished from the teachings of Bauer *et al.* in being directed to products and methods practiced in plants, which

argument is not persuasive with regard to Bauer *et al.* in view of Ow because the teaching of reporter gene excision practiced in plants is provided by Ow and for the reasons stated herein above, would be obvious to one of ordinary skill in the art in view of the teachings of Bauer *et al.* and Ow.

Applicant further argues that the instant claims are distinguished from Bauer *et al.* because Bauer *et al.* states in the abstract of the disclosure that the direct repeat sequences are "non exogenous" while the instant claims have been amended to recite that the direct repeats comprised by the construct are of a "non-native gene of interest with respect to the host plant cells".

This argument has been fully considered but is not deemed persuasive. Applicant appears to be construing the statement in the abstract of Bauer *et al.* as requiring that the direct repeat sequences be "native" to the host cell. However, as stated in the first full paragraph on page 3 of the 24 June Office Action (emphasis added), "It should be noted that Bauer *et al.* teaches that the DRS sequences can be 'yeast DNA sequences not present in the host strain' (column 6, line 51). Thus, Bauer, *et al.* teaches that the DRSs can be heterologous genes that are heterologous to the host cell genome". Furthermore, in the paragraph bridging column 6-7 and the first full paragraph in column 7, Bauer *et al.* teaches, "After excision, one of the 2 DRS sequences remains in place in the genome; it is therefore necessary that this sequence consists of yeast DNA, that is to say DNA belonging to the same genus and preferably the same species yeast. As was indicated above, it is also possible to use, as DRS sequences, fragments of a yeast gene which is absent for the industrial yeast host strain to be transformed" (emphasis added). In view of these teachings, it is clear that by "non exogenous" Bauer *et al.* does not mean that the DRS

sequence must be "native" to the specific host cell being transformed but that the DRS sequence should be non exogenous to the genus or species of organism being transformed. Thus, the recitation that the direct repeats be "of a non-native gene of interest with respect to the host plant cells" does not distinguish the claimed invention from the teachings of the cited art.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole; therefore, the claims stand rejected under 35 USC §103(a) as unpatentable over the art.

New Grounds Necessitated by Amendment

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The claims recite the limitation "non-native gene of interest with respect to the plant cells". The specification does not provide antecedent basis for this limitation. Applicant should delete the limitation or amend the specification to provide antecedent basis while being careful not to introduce new matter into the disclosure.

Claim Objections

Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. Specifically, claim 17 limits the eukaryotic cell of claim 4 to a plant cell; however, claim 4, as amended is already limited to practice with plant cells.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, 7 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claim 1, which was previously directed to "a genetic construct" comprising a positive selectable marker, a negative selectable marker and two direct repeats of a gene of interest immediately flanking the positive and negative selectable marker genes, has been amended such that it is directed to "a genetic construct system" comprising those elements. Throughout, the disclosure contemplates the positive selectable marker, the negative selectable marker and the direct repeats being present on a single genetic construct, which is required for the uses contemplated in the specification (*i.e.*, delivery of a nucleic acid comprising the selectable markers and selection for excision of the selectable markers by positive/negative selection). However, as the amended claim 1 is directed to a "genetic construct system" the claims can now be construed as encompassing any system comprising a genetic construct or

constructs comprising the recited elements either on a single construct or on multiple different constructs. For example, a system comprising two constructs, one of which comprises a positive selectable marker flanked by two direct repeats and one of which comprises a negative selectable marker flanked by two direct repeats is now within the scope of the claims. As the originally filed disclosure did not contemplate "a genetic construct system" as presently claimed, the amended claims encompass impermissible new matter.

It is noted that this rejection could be overcome by structuring the claim such that the genetic construct system is directed to comprising: i) a genetic construct comprising: a. a positive selectable marker [etc.]; and ii) the host plant cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 10-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4 are indefinite in reciting the limitation, "a non-native gene of interest with respect to the host plant cells". The specification does not contain a definition of "non-native gene" and the metes and bounds of the limitation are unclear from the description.

In the remarks, Applicant cites paragraph 36 of the published application as providing support for the limitation. Paragraph 35 reads as follows:

> **[0036]** A "gene of interest" or "GI", and the "additional genes" or "AG", include, but are not limited to, genes which are not normally present in the transformed plant. This includes DNA sequences not normally transcribed into RNA or translated into a protein ("expressed"), or any other genes or DNA sequences which one desires to introduce into the non-transformed plant, such as genes that may normally be present in the non-transformed plant, but which one desires to either genetically engineer or to alter the expression thereof.

The cited teaching does not use the term "non-native" or indicate that what is described therein is a gene that is "non-native" with respect to the host plant. Given the standard meaning of the term "non-native", the skilled artisan would interpret the phrase as limited to genes that are not normally present in the genome of the host plant. However, the cited teaching suggests that the gene of interest might be a gene that is present in the genome but not transcribed into RNA, might be a gene that is transcribed into RNA but not translated into protein, or genes that may normally be present in the host cell but which one desires to engineer. It is thus unclear whether the term "non-native" is limited to what would be the standard meaning in the art or whether the passage cited by Applicant is meant to define the term in a more generic way. In view of the fact that the original disclosure does not use the term "non-native" and the metes and bounds of the term, interpreted in light of the specification are not clear, the metes and bounds of the claims as a whole are unclear.

Claims 2, 3, 5-7 and 10-18 are indefinite insofar as they depend from independent claims 1 or 4.

Allowable Subject Matter

Claims 8, 9 and 19-21 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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